

EXOPHTHALMIC GOITRE.¹ (14)

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DURING the last two years I have had under my observation five cases of exophthalmic goitre, and I have had the exceptional experience of two necropsies—one on a case of my own and the other on a case of Dr. Davidson at the Infirmary. I shall divide the remarks I have to make into three groups—viz., (1) the symptoms; (2) the morbid anatomy and pathology; and (3) prognosis and treatment.

1. *Symptoms.*—The onset may be acute or chronic, the course short or prolonged over years. The earlier symptoms are associated with the cardio-vascular system and consist chiefly of a persistent tachycardia. Occasional attacks of palpitation are present. Physical examination reveals a diffused cardiac impulse, with enlargement of the area of cardiac dullness. Functional bruits are common. The arteries in the neck are dilated, and visible pulsation in them is common. The radial pulse is frequent and of low tension; the frequency may be 150 to 200 per second. Goitre follows and consists of a firm enlargement of the gland, usually more marked upon the right side. The goitre is painless, and, in my experience, is not pulsatile. A rough systolic murmur is usually audible in the neighbourhood of the gland. Exophthalmos may be a very late symptom. Other eye symptoms are defective descent and retraction of the upper lid. In one case I noted a symptom first recorded by Joffroy—viz., a loss of the contraction of the frontalis muscle associated with the sudden upward movement of the eyes. The pupils in my cases, with one exception, were not dilated. To the so-called cardinal symptoms another should be added—viz., muscular tremor. It was present in all my cases, and is, I believe, a constant and early symptom of the disease. The tremor has been thoroughly investigated by Marie,² who states that it may be best brought out by getting the patient to hold the arms in the extended position. The narrow excursions and the rapidity ($8\frac{1}{2}$ per second) distinguish the tremor from other forms; that of alcoholism, which most resembles it, may be recognised by the irregularity both of time and excursions. The general features of the disease are familiar, and may be, therefore, very briefly given. They are emaciation, anaemia, irregular rises of temperature, flushings and sweatings, diarrhoea, and excitable mental state, passing on to actual insanity. Amenorrhoea is a constant feature in women. Diminution of the electrical resistance of the skin is said to be a constant phenomenon. In a few cases general enlargement of the lymphatic glands has been observed, and in both the necropsies I have made the lymphoid follicles in the intestines were swollen. Dr. Hunt informs me that he has twice operated for enlarged tonsils in cases of Graves' disease. In both cases the enlargement took place after the onset of the latter. Rarer symptoms are various forms of paralysis, glycosuria, albuminuria, and oedema. The termination may be in recovery or death from exhaustion or syncope.

With this brief account of the clinical features I pass on to consider my second group.

2. *Morbid anatomy and pathology.*—The older theories of Stokes and Graves (primary cardiac) and Marshall and Taylor (pressure on nerves and vessels of neck) have been long abandoned. The sympathetic theory must, I think, now be given up also. The tachycardia and the vascular dilatation at first sight suggest a lesion of the sympathetic nervous system. On closer examination it is found, as Gowers points out,³ that this theory involves the assumption of (a) a partial affection, or (b) a twofold action—viz., a stimulating one upon the accelerating fibres of the heart and a paralysing one upon the vaso-motor fibres—a double-barrelled action the probability of which is rather remote. Again, if there were a sympathetic lesion we should expect dilatation of the pupils to be a common symptom, whereas it is rare. It was only present in one of

my five cases. Moreover, the sympathetic system in the neck has been found to be normal in the vast majority of the fatal cases. In thirteen cases recorded by Lewin⁴ it was normal in all. It was normal in both my cases. A much more probable theory is one which locates the lesion in the central nervous system, and more especially in the medulla. The association of arterial dilatation with increased frequency of the heart's action is in harmony with Marey's well-known law that "there is an inverse ratio between pulse frequency and blood pressure in consequence of their relationship to a central mechanism." Filehne, and Durduti, in repeating Filehne's experiments, have shown that division of the restiform body gives rise to symptoms closely resembling those of exophthalmic goitre. There is no doubt, too, that in some cases, more especially the acute ones, lesions have been found in the medulla—e.g., increased vascularity by Greenfield⁵ and myself, hæmorrhages by Müller,⁶ Hale White, Stewart and Gibson,⁷ and abscess by Stewart and Gibson.⁸ The usual absence of anatomical changes and the undoubted presence of a marked neurotic inheritance led Charcot to regard the disease as a neurosis, and to this phase of the nervous theory I shall allude again. For my own part, I fail to see how a lesion in the medulla can give rise to the psychical and paralytic symptoms so commonly met with in this disease. It is probable that the cardio-vascular phenomena are due to a disturbance of the medullary centres, but that this disturbance is secondary and not primary. The nervous system theory is still accepted by many writers (Mannheim⁹ and others), but the latest, and at present, I think, the most satisfactory, theory is the one which attributes the disease to a primary lesion of the thyroid gland. In considering the affection from this aspect the thyroid gland must be dealt with first. The examination of the goitre in my two cases revealed a condition which was in striking contrast to that usually described. The condition I found corresponds closely to that recorded as present in their cases by Stewart and Gibson,¹⁰ Greenfield,¹¹ O. Hezel,¹² Joffroy,¹³ and Putnam.¹⁴ The thyroid gland was enlarged; the alveoli were small and apparently more numerous, they were packed with cells, and the colloid material was absent. In one of my cases (acute) there were masses of leucocytes at the points of entrance of the larger vessels. In chronic cases an overgrowth of connective tissue has been present, with some tendency to cyst formation. It will be noticed that in this description there is no allusion to any marked increase of vascularity. Is the goitre a vascular one? From the clinical side I must say that in my five cases repeated examinations failed to detect any expansile pulsation in the goitre, and the histological examination of my own case and under Dr. Davidson's care confirms me in the belief that the goitre is not a vascular one. Of course, some increase in vascularity is necessarily present in an over-active gland, but my point is that there is nothing approaching an aneurysmal condition, and therefore the goitre in Graves' disease is not clinically a pulsatile one.¹⁵ The marked thrill and bruit present in these cases are due to vibrations in the main thyroid arteries and not in the gland itself. It is important to note that the histological characters described above are present even when the gland during life is not appreciably enlarged—a point of great interest in connexion with cases of persistent tachycardia, which many observers would class as *fruste* examples of Graves' disease. Greenfield¹⁶ compares the histological characters to those seen in an active mammary gland, and suggests that the thyroid gland in these cases is in a state of over-activity. Some support is lent to this suggestion by the fact that the gland tissue in Graves' disease bears a close resemblance to the thyroid tissue in early life, when the gland is supposed to be in a state of great activity.¹⁷ Assuming, as I think is permissible, that the thyroid gland

⁴ Inaugural Dissertation, Berlin, 1888.

⁵ Bradshaw Lectures, THE LANCET, Dec. 16th, 1893.

⁶ Deutsches Archiv für Klinische Medizin, Band xli.

⁷ Brit. Med. Jour., Sept. 23rd, 1893.

⁸ Ibid.

⁹ Morbus Gravesii. Berlin, 1894.

¹⁰ Brit. Med. Jour., Sept. 23rd, 1893.

¹¹ THE LANCET, Dec. 16th, 1893.

¹² Deutsche Zeitschrift für Nervenheilkunde, 1873.

¹³ Progrès Médical, December, 1894.

¹⁴ American Journal for Nervous and Mental Diseases, December, 1893.

¹⁵ My point is sustained by a case of Mr. Paul, in which, when the isthmus was divided in the operation of partial thyroidectomy for Graves' disease, no bleeding of any moment took place.

¹⁶ THE LANCET, Dec. 16th, 1893.

¹⁷ Professor Sherrington informs me that after partial thyroidectomy the remaining gland tissue assumes the character of that seen in Graves' disease—a fact which gives additional and strong support to Greenfield's suggestion.

¹ A paper read before the Medical Institution of Liverpool on Oct. 17th, 1895.

² Contribution à l'Étude des Formes frustes de la Maladie de Basedow. Paris, 1883.

³ Diseases of the Nervous System, vol. ii., p. 385.

is over-active in these cases, it has yet to be shown that excess of thyroid secretion can give rise to the symptoms of the disease. The symptoms of thyroidism in the human subject bear a very close resemblance to those of exophthalmic goitre—emaciation, sweating, frequent pulse, tremors, excitable nervous system, and exophthalmos¹⁸ have all been observed. Again, the contrast between the symptoms of myxœdema, which it is universally acknowledged are due to the absence of thyroid secretion, and those of exophthalmic goitre, which it is suggested are due to an excess of thyroid secretion, is very marked, as will be seen by the following comparison:—

	Myxœdema.	Exophthalmic Goitre.
Thyroid gland	Atrophy	Hypertrophy.
Sweating	Absent	Copious.
Temperature	Subnormal	Often raised.
Sensation	Of cold	Of heat.
Electric resistance of skin...	Increased	Diminished.
Pulse	Infrequent	Frequent.
Mental and bodily state.....	Sluggish	Excitable.

Further support is lent to the thyroid gland view by the fact that in some twelve cases recorded by Ord and others the symptoms of Graves' disease have been followed by those of myxœdema. The intimate connexion between the thyroid gland and exophthalmic goitre is still further emphasised by the favourable results following operations which lessen the amount of secreting gland tissue.

—	Number of cases.	Improvement.	Recovery.	Death.
Putnam ¹⁹	51	34	13	4
Wette ²⁰	30	28	—	—
Lemke ²¹	8	3	4	—
Krönlein ²²	8	8	—	—
Kocher ²³	39	39	—	—
Tillaux ²⁴	2	2	—	—

It seems, therefore, that there is much probability in the view that exophthalmic goitre is a thyroid disease and that the symptoms are due to an excess of thyroid secretion in the blood. Mr. Edmunds,²⁵ on experimental grounds, seems to incline to the sympathetic theory, but upon this I need not touch again. He raises the question as to whether the disease is due to an excess of normal secretion or to a perverted secretion. No doubt the injection of cocaine produces many, if not all, of the symptoms of exophthalmic goitre, but it appears to me that, inasmuch as normal thyroid juice will give rise to all the symptoms of the disease, it is unnecessary to assume the existence of any poison akin to cocaine.

Before dealing with the question of prognosis and treatment I must add a word with regard to the eye symptoms. Exophthalmos is frequently a very late symptom, and is, I believe, due to the dilatation of the retro-bulbar vessels. In one of my cases it disappeared during an attack of diarrhoea, to return when the diarrhoea ceased. In the fatal cases I examined no appreciable increase of intra-orbital fat could be made out, and it has always been a matter of wonder to me why this suggestion should have been made in view of the fact that emaciation is a marked feature of the disease. The external ocular muscles were pale, but not obviously fatty; Müller's muscle I could not find in one case. The mechanism of Von Graefe's and Stellwag's symptoms is no doubt nervous, but as to the exact nature thereof I have no suggestion to offer.

3 *Prognosis and treatment.*—Gowers²⁶ says "that in few diseases of equal severity and corresponding apparent gravity is the prognosis so uncertain, and that in well-marked cases little or no improvement has followed the most careful treatment." With the first clause of this statement all will agree, but it is probable that the thyroid theory of the disease may lead us to reconsider the second. Briefly put, the routine treatment has consisted in rest in the recumbent posture and quiet surroundings, and in four of my cases this was sufficient to enable the patients to go back to work. The late Mr. Denton Cardew strongly recommended electrical

treatment, and Nothnagel speaks very highly of the effect of mountain residence. Drugs, in my experience, do but little good, although it is interesting to note the reputed value of belladonna from its well-known action on the salivary glands. Although I have no personal experience to offer, yet it seems to me, from the results I have submitted, that in operations intended to diminish the amount of thyroid gland tissue there exists a new and better prospect of affording relief, if not cure, to the subjects of Graves' disease. Two operations seem to have stood the test of trial. They are (1) partial thyroidectomy. The right lobe only has usually been removed, in all the cases in my list, with the exception of Kocher's. (2) Ligature of the thyroid arteries. This was the operation selected by Kocher and is based upon the experimental work of Tarchanof, who has shown that ligature of the thyroid arteries leads to atrophy of the gland. In Kocher's cases three out of the four main arteries were tied.

A few words must be added with regard to the etiological side of the question. There is little definitely known, so I shall just touch upon the two points which are emphasised in all the text-books. The first is that in the majority, if not in all, of the cases there is a marked neurotic inheritance. I made this out in all my cases. The second is that emotional disturbance is a prominent exciting cause. This was certainly not so in my own cases, and it is probable that in the cases attributed to emotional disturbance the affection has been present, though unnoticed, and that emotion simply caused an exacerbation of symptoms which brought the patient under observation. The intimate relationship between the thyroid gland and the central nervous system has been established beyond all doubt by the experimental work of Horsley and others, and, therefore, it is impossible to deny absolutely that the thyroid changes are dependent upon a primary nervous lesion. It seems probable that, even admitting this, the symptoms are brought about by excessive thyroid activity.

In conclusion I would urge that the important link in the chain of phenomena called "exophthalmic goitre" is the thyroid gland, and that it is to the breaking of this link that we must direct our efforts for the removal of the symptoms of the disease.

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A NOTE ON

CYSTIC DEGENERATION OF THE MAMMÆ, WITH THREE CASES OF "RECURRENCE" ON THE OPPOSITE SIDE.

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ALTHOUGH one not seldom hears a breast tumour spoken of as "a simple cyst," I desire to point out that such a lesion very rarely, if ever, occurs in women verging on middle age, when the organ is entering its devolution epoch. In the young a dilated milk-duct is often seen as the result of obstruction, and may well be thus described. After the age of thirty-four cyst formation is, in my experience, invariably due to a general aberration in the devolution of the entire parenchyma, not merely of one but, as the following cases show, of both mammæ. There may be found but a single cyst of appreciable size; with this, however, are always associated numerous others, possibly hardly larger than a pin's head, uniformly distributed throughout the gland tissue. If not operatively interfered with the condition may continue until the entire mamma becomes a congeries of cysts, within which, sooner or later, "intracystic vegetations," carcinomatous or sarcomatous, develop. It is brought about, like cancer, by any emotional or mechanical hindrance to the natural processes, whereby the mammæ pass to their obsolete phase. When there is redundant formation of white fibrous tissue between the cysts the tumour is spoken of as a "cystic fibroma"; but there is no essential difference between this and the simpler cystic degeneration. It is best when operating carefully to remove the whole breast tissue, and if questioned, as commonly happens, about possible "recurrence" to give a guarded prognosis so far as concerns the remaining organ. The point that we have here to deal with a general and not merely a local lesion of the

¹⁸ Bécierre: Archives Générales de Médecine, February, 1895.

¹⁹ Loc. cit. ²⁰ Archiv für Klinische Chirurgie, Band xlv., 1892, p. 44.

²¹ Deutsche Medicinische Wochenschrift, No. 42, 1894.

²² Correspondenz-Blatt für Schweizerische Aerzte, No. 15, 1894.

²³ Ibid., January, 1895.

²⁴ Traité d'Anatomie Topographique, p. 426 and footnote.

²⁵ Transactions of the Pathological Society of London, 1895, p. 224.

²⁶ Loc. cit., vol. ii., p. 891.